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EXAMINER

GEISEL, KARA E

ART UNIT PAPER NUMBER

2877

DATE MAILED: 06/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/869,317

Applicant(s)

GERSTNER ET AL.

Examiner

Kara E Geisel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6-8, 21, 23-29 and 32-38 is/are allowed.
- 6) ☒ Claim(s) 1-4, 9-11, 15, 16, 19, 20, 22, 30 and 31 is/are rejected.
- 7) ☒ Claim(s) 5, 12-14, 17-18 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 21 December 2001 is: a) ☒ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6-7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Preliminary Amendment

The preliminary amendment filed on December 21st, 2001, and the substitute specification has been entered into this application.

Information Disclosure Statements

The information disclosure statements filed on February 21st, 2002, July 25th, 2002, and September 26th, 2002 has been fully considered by the examiner.

Drawings

The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on December 21st, 2001, has been approved. A proper drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The correction to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4, 11, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Morgan (USPN 5,459,323), as cited by the applicant.

In regards to claim 1, Morgan discloses a process for detecting the phenomenon of fluorescence in a microscope (column 1, lines 1-10) comprising the steps of irradiating a sample by at least one of a modulated and a pulsed light source (column 2, lines 49-53), wherein the light source can be a laser (column 7, lines 65-67) so as to produce fluorescence (column 4, lines 58-61), and detecting the

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fluorescence with a detector (fig. 10, 203-204) having variable phase positions at least in two different phase positions of the detector (column 10, lines 42-63).

In regards to claim 2, Morgan's process further comprises the step of generating an image for each phase position using a signal output by the detector (column 10, lines 32-63).

In regards to claim 4, the process by Morgan can be carried out using a laser-scanning microscope (column 7-8, lines 62-67 and 1-5, respectively and column 12, lines 41-45).

In regards to claim 11, the irradiating step can be carried out using a cw laser modulated by means of a Pockel cell (column 1, lines 54-60).

In regards to claim 20, the process further comprises a step of carrying out a mathematical algorithm on the image to produce another image (column 9, lines 15-33).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 3 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan (USPN 5,459,323), as cited by the applicant.

In regards to claim 3, Morgan discloses a process for detecting the phenomenon of fluorescence in a microscope, as discussed above. Although Morgan does not disclose that the image for each phase position is displayed on a monitor, it is obvious to one skilled in the art that the images could be displayed on a monitor in order to view the images, and furthermore, that Morgan has the ability to do so, since images of the sample at different phases are shown in figures 8-9 and 11a-12b.

In regards to claim 19, it is very well known in the art to use phase sensitive detection to improve the signal to noise ratio and it would be obvious to one of ordinary skill in the art to use phase sensitive detection in this system.

Claims 9, 15-16, 22, and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan (USPN 5,459,323), as cited by the applicant and as applied to claims 1-4 and 11 above, in view of Denk et al. (USPN 5,034,613).

In regards to claim 9, Morgan discloses a process for detecting the phenomenon of fluorescence in a microscope, as discussed above. Morgan does not disclose that the irradiating step is carried out using multi-photon excitation of fluorescence emission. However, multi-photon excitation is well known in the art, has many advantages, and it would be obvious to one of ordinary skill in the art to use multi-photon excitation in this system.

For example, Denk discloses a laser-scanning microscope that constructs images of a sample by irradiating using a pulsed laser to produce multiphoton excitation of fluorescence emission (abstract). This is done to provide improved background discrimination and reduce photobleaching (column 2-3, lines 31-68 and 1-30, respectively). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the pulsed light source of Morgan's system to produce

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multi-photon excitation of fluorescence emission in order to improve background discrimination and reduce photobleaching.

In regards to claim 15, the combined system using a multiphoton process is discussed above. Furthermore, Morgan's system detects using time resolution (column 11, lines 30-39).

In regards to claim 16, Morgan discloses a process for detecting the phenomenon of fluorescence in a microscope, as discussed above. Morgan does not disclose that the irradiating step is carried out using a near infrared laser. However, in order to cause a fluorophore that fluoresces in UV to fluoresce by two-photon excitation, a laser beam of high instantaneous power and long wavelength, such as near infrared is needed (Denk, columns 5-6, lines 62-68 and 1-30, respectively). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a pulsed near infrared laser in the combined system.

In regards to claim 30, second harmonic generation is well known in the art, and would be obvious to one of ordinary skill in the art to have second harmonic generation on surfaces as the multiphoton process.

In regards to claims 22 and 31, the multi-photon process is a two-photon excitation (Denk column 2, lines 31-35).

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan (USPN 5,459,323), as cited by the applicant and as applied to claims 1-4 and 11 above, in view of Lakowicz et al. (USPN 5,504,337).

In regards to claim 10, Morgan discloses a process for detecting the phenomenon of fluorescence in a microscope, as discussed above. Morgan does not disclose using a cw laser modulated by means of an acousto-optical modulator. However, modulating a laser beam by this method is well known in the art, and would be obvious to do to one of ordinary skill in the art.

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For example, Lakowicz discloses an apparatus for measuring the lifetimes of fluorescence emitted by a sample (column 4, lines 43-50) by phase angle (column 5, lines 3-10). Lacowicz discloses many types of pulsed or modulated light sources for use in measuring the lifetime of a fluorescence sample, including a cw laser that can be pulsed by an acousto-optic modulator (column 9, lines 5-41). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a cw laser source pulsed by an acousto-optic modulator as an alternative source in Morgan's device.

Allowable Subject Matter

Claims 6-8, 21, 23-29, and 32-38 are allowed over the prior art of record.

Claims 5, 17-18 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter:

As to claim 5, the prior art of record, taken alone or in combination, fails to disclose or render obvious a process for detecting the phenomenon of fluorescence in a microscope comprising detecting fluorescence using a modulatable PMT, in combination with the rest of the limitations of claim 5.

As to claim 6, the prior art of record, taken alone or in combination, fails to disclose or render obvious a process for detecting the phenomenon of fluorescence in a microscope comprising multiplying a reference signal and a measurement signal which have a fixed variable phase relation, to obtain a result, in combination with the rest of the limitations of claim 6.

As to claims 12-14, the prior art of record, taken alone or in combination, fails to disclose or render obvious a process for detecting the phenomenon of fluorescence in a microscope comprising irradiating using a pulsed laser that is additionally modulated, in combination with the rest of the limitations of claims 12-14.

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As to claims 17-18, the prior art of record, taken alone or in combination, fails to disclose or render obvious a process for detecting the phenomenon of fluorescence in a microscope comprising converting the frequency of the laser downstream to one photon excitation, in combination with the rest of the limitations of claims 17-18.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kara E Geisel whose telephone number is 703 305 7182. The examiner can normally be reached on Monday through Friday, 8am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frank Font can be reached on 703 308 4881. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872 9318 for regular communications and 703 872 9319 for After Final communications. For inquiries of a general nature, the Customer Service fax number is 703 872 9317.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1782.



F.L. Evans
Primary Examiner
Art Unit 2877



KEG
May 30, 2003